Sulfuric Acid, Diethyl Ester

(Diethyl Sulfate; CAS RN 64-67-5)

High Production Volume (HPV) Chemical Challenge Final Test Status and Data Review

Prepared for:

The Dow Chemical Company

Prepared by:

Toxicology/Regulatory Services, Inc.

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Final Test Status

Sulfuric Acid, Diethyl Ester (Diethyl Sulfate; CAS RN: 64-67-5)		Information	OECD Study	GLP	Other Study	Estimation Method	Acceptable	Testing Required
STUDY		**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**	**Y/N**
PHYSICAL AND CHEMICAL DATA								
2.1	Melting Point	Y	N	N	Y	N	Y	N
2.2	Boiling Point	Y	N	N	Y	N	Y	N
2.4	Vapor Pressure	Y	N	N	Y	N	Y	N
2.5	Partition Coefficient	Y	N	N	N	Y	Y	N
2.6	Water Solubility	Y	N	N	Y	N	Y	N
ENVIRONMENTAL FATE AND PATHWAY								
3.1.1	Photodegradation	Y	N	N	N	Y	Y	N
3.1.2	Stability in Water	Y	Y	Y	N	N	Y	N
3.3	Transport and Distribution	Y	N	N	N	Y	Y	N
3.5	Biodegradation	Y	N	N	Y	N	Y	N
ECOTOXICITY								
4.1	Acute Toxicity to Fish	Y	Y	Y	Y	N	Y	N
4.2	Toxicity to Daphnia	Y	Y	Y	N	Y	Y	N
4.3	Acute Toxicity to Algae	Y	Y	Y	N	Y	Y	N
TOXICITY								
5.1	Acute Toxicity	Y	N	N	Y	N	Y	N
5.4	Repeated Dose Toxicity	Y	N	N	Y	N	Y	N
5.5	Genotoxicity *In Vitro* (Bacterial Test)	Y	N	N	Y	N	Y	N
5.5	Genotoxicity *In Vitro* (Mammalian Cells)	Y	N	Y	Y	N	Y	N
5.8	Reproductive Toxicity	Y	N	N	Y	N	Y	N
5.9	Development Toxicity / Teratogenicity	Y	N	N	Y	N	Y	N

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1.0 Introduction

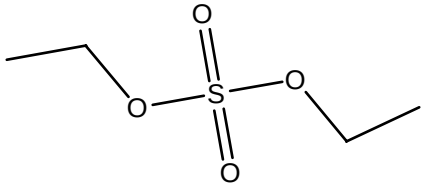
This document reviews the data availability for the High Production Volume (HPV) Chemical Challenge endpoints and provides a Test Plan for Sulfuric Acid, Diethyl Ester, hereafter called Diethyl Sulfate [DES; CAS RN 64-67-5]. DES is sponsored by The Dow Chemical Company. DES is classified as a carcinogen by IARC (2A; "Probably carcinogenic to humans") and NTP ("Anticipated carcinogen"). As a suspect human carcinogen, exposure is strictly controlled. Since DES is ultimately hydrolyzed to ethanol and sulfuric acid, data for these chemicals has been included in this Final Test Status and Dossier to help fulfill several endpoints. As stated in the original Test Plan, however, the submitter reiterates that the controls required in production and use of DES (resulting from its carcinogenicity) adequately protect for repeat exposure, reproductive, and developmental toxicity.

2.0 General Use and Exposure

Diethyl sulfate is a versatile alkylating agent for producing ethyl derivatives of many compounds such as amines, phenols, and thiols. It is used in the preparation of a wide variety of intermediates and products in surfactants, dyes, agricultural chemicals, and pharmaceuticals. The major use of diethyl sulfate is in the manufacture of quaternary ammonium salts that are used in: textile applications for fabric softeners in detergents and for dye operations to increase the affinity of the dye for the fiber; hair care applications for shampoos, conditioners and hair spray; germicides for disinfectants and sanitizers in a broad range of products including cleaners, drilling fluids, and cooling water applications; and production of organoclays for viscosity modifiers in drilling fluids, greases, lubricants, and oil based paints, phase transfer catalysts, electroplating, emulsifying agents including asphalt additives, and corrosion inhibitors. Other uses include production of ethers from alcohols; to produce fatty acid ethyl esters for plasticizers and to alkylate substituted aniline for dyes; and as a pharmaceutical intermediate. Production in the U.S. was in the range of 0.5 to 1 million pounds in 2002.

Approximately 194 full-shift samples were collected from 1978 to 1996 at a US production site. All results ranged between none-detected (limit of detection 0.01 ppm) and 0.7 ppm. There were no results greater than the established internal exposure guideline of 1 ppm as an 8-hr TWA. Samples were collected from a variety of tasks including drumming activities, work at a loading rack, and other routine tasks. Thirty short-term samples were collected from 1975 to 1987. Results ranged from one-detected (limit of detection 0.01) to 1.8 ppm. Samples were collected during drumming operations, filter changes, and connecting and disconnecting hoses. Therefore, exposure in the workplace is considered to be of no concern and appropriate measures are taken to avoid worker contact. In addition, based on its use as a chemical intermediate and the rapid hydrolysis of any residual DES from production, no significant exposure to consumers is anticipated to occur.

3.0 General Substance Information (Identity)

Chemical Name	Sulfuric Acid, Diethyl Ester
Synonyms	Diethyl Sulfate Diaethylsulfat [German] Diethyl sulphate Diethyl tetraoxosulfate Diethylester kyseliny sirove [Czech] Ethyl sulfate
CAS Number	64-67-5
Structure	
Molecular Weight	154.18
Substance Type	Organic
Physical State	Colorless liquid
Odor	Mild
Purity	>99%

4.0 Physical/Chemical Properties

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

4.1 Melting Point

The melting point for DES is listed as -24.5 ºC (CRC Press, 1975). The Material Safety Data Sheet indicates the freezing point to be -24.4 ºC. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.2 Boiling Point

The boiling point for DES is listed as 208 ºC (CRC Press, 1975). The Material Safety Data Sheet indicates that DES decomposes at high temperatures. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.3 Vapor Pressure

The vapor pressure for DES is listed as 0.191 hPa at 20 ºC (DIPPR, 2000). This value is considered adequate to meet the HPV Chemical Challenge requirements.

4.4 Partition Coefficient

The log K_{ow} for DES is predicted by EPIWIN to be 1.14 (U.S. EPA, 2000a). An unpublished reference from Union Carbide provides the same value (Union Carbide; unpublished data). Because of the rapid hydrolysis of DES in water (see below), this value has minimal utility in determining its environmental fate or bioaccumulation in aqueous systems. However, the low value indicates bioaccumulation is not anticipated. These data are considered adequate to meet the HPV Chemical Challenge requirements.

4.5 Water Solubility

DES rapidly hydrolyzes to ethanol and H_2SO_4 (CRC Press, 1975). A water solubility value of 7000 mg/L has been determined (McCormack and Lawes, 1983). The rate at which the hydrolysis occurs has not been adequately addressed. The value of 7000 mg/L is considered an adequate determination of water solubility for the HPV Chemical Challenge requirement and for the conduct of the water stability study (see below).

5.0 Environmental Fate

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

5.1 Photodegradation

The model prediction for atmospheric photodegradation provides a second order rate of reaction with hydroxyl radicals of 1.6 E-12 cm^3/molecule-sec and a $t_{1/2}$ of 6.5 days (U.S. EPA, 2000b). Because of the nature of use of DES, photodegradation is of minimal importance to the overall environmental fate. Degradation from accidental release to the atmosphere, however, is anticipated based on the modeling. These data are considered adequate to meet the HPV Chemical Challenge requirements.

5.2 Stability in Water

A study examining the hydrolysis of DES as a function of pH was performed according to the OECD Guideline 111 (Erhardt, 2006). DES was added to the buffer solutions at 1500 mg/L (pH 4 and 7) and 1520 mg/L (pH 9) and incubated at 50ºC. After two hours, 1.8% (pH 4), 1.7% (pH 7) and 0% (pH 9) of the initial test material concentrations remained and none was detected after 5 days. The hydrolysis half-lives at 50ºC were estimated to be 0.35 hours for pH 4 and 7, and 0.19 hours for pH 9. Since the half-life of DES was determined to be less than 2.4 hours at 50ºC, the extrapolated half-life at 25ºC is estimated to be less than 24 hours, as per the guideline. These half-lives indicate that DES was sufficiently unstable such that further evaluation of the hydrolysis kinetics was not warranted. Based upon these results, the half-life of DES at 25ºC at pH7 was predicted to be 1.9 hours. Primary hydrolysis of DES was expected to yield one mole each of ethyl sulfuric acid and ethanol for each mole of DES hydrolyzed, which was confirmed by analytical analysis. After five days of incubation at 50ºC, concentrations of both ethyl sulfuric acid and ethanol remained relatively stable and no sulfate formation was observed in the reaction solutions. Therefore, the rapid initial hydrolysis of DES results in the formation of ethyl sulfuric acid and ethanol as stable

hydrolysis products ($t_{1/2}$ < 0.4 hours at 25ºC) and ethyl sulfuric acid is relatively resistant to hydrolysis ($t_{1/2}$ > 1 year at 25ºC).

5.3 Environmental Transport and Distribution

The Level III fugacity model (U.S. EPA, 2000c) was used to predict the distribution of DES released to the environment. DES is not routinely released to the environment because of the controls in place to avoid human exposure and because it is used exclusively as a chemical intermediate. Therefore, only accidental releases were considered for the fugacity modeling. Two scenarios, 100% release to air and 100% release to water were examined. For the air release the model predicted a distribution of 77% into atmosphere, 15% into water, 9% into soil, and < 0.1% into sediment. For the water release the model predicted a distribution of < 1% into atmosphere, 99% into water, < 0.1% into soil, and < 1% into sediment. These data are considered adequate to meet the HPV Chemical Challenge requirements.

5.4 Biodegradability

A study measuring the Biological Oxygen Demand provided a value of 57% degradation after 20 days (Price *et al.*, 1974). A second biodegradation study with DES performed according to OECD Guideline 301C indicated 89% degradation after 28 days (Chemicals Inspection & Testing Institute, Japan, 1992). These data are considered adequate to meet the HPV Chemical Challenge requirements.

6.0 Ecotoxicity

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

6.1 Toxicity to Fish

An acute toxicity study of ethane sulfuric acid was performed with rainbow trout, *Oncorhynchus mykiss*, according to the OECD Guideline 203, the EEC Directive C.1 and the U.S. EPA TSCA Guideline 40 CFR 797.1440 (Marino *et al.*, 2005b). Rainbow trout were exposed to 0 (water control) and 1000 mg ethanesulfuric acid/l (limit concentration) for 96 hours under static conditions. Concentrations of ethanesulfuric acid were measured within all replicate control and treatment solutions on Days 0 and 4. The mean measured concentrations were less then the LOQ of 47.3 mg/L for the water control and 952 mg/L for the 1000 mg/L nominal treatment level. There was no mortality over the 96 hours. The 24-, 48-, 72- and 96-hour LC_{50} values were >952 mg/L, the mean measured limit concentration tested. The 96-hour NOEC was 952 mg/L, the mean measured limit concentration that exhibited no mortality or sublethal effects.

6.2 Toxicity to Aquatic Invertebrates

An acute toxicity study of the primary hydrolysis product of DES, ethanesulfuric acid, was performed with the freshwater daphnid, *Daphnia magna*, according to the OECD Guideline 202, the EEC Directive C.2 and the U.S. EPA TSCA Guideline 40 CFR 797.1300 (Marino *et al.*, 2005a). The daphnids were exposed to 0 (water control) and 1000 mg ethanesulfuric acid/L (limit concentration) for 48 hours under static conditions. Concentrations of

ethanesulfuric acid were measured within all replicate control and treatment solutions on Days 0 and 2. The mean measured concentration was 914 mg/L for the 1000 mg/L nominal treatment level. The 24- and 48-hour LC_{50} values were >914 mg/L, the mean measured limit concentration tested. The 48-hour NOAEC was estimated to be 914 mg/L, the mean measured limit concentration that exhibited no immobility or change in behavior or appearance.

6.3 Toxicity to Aquatic Plants

An algal growth inhibition assay was conducted with the primary hydrolysis product of DES, ethanesulfuric acid, according to the OECD Guideline 201, the EEC Directive C.3 and the U.S. EPA TSCA Guidelines, 40 CFR 797.1050 (Hancock *et al.,* 2005). In-house cultures of *Pseudokirchneriella subcapitata*) were exposed to 0, 62.5, 125, 250, 500, 1000 and 2000 mg ethanesulfuric acid/L of algal assay medium (AAM) for 72 hours and evaluated for effects on cell density, specific growth rate and biomass area. Mean measured exposure concentrations were 0, 60.1, 118, 247, 504, 1001 and 1958 mg ethanesulfuric/L which corresponded to 95.8 to 104% of the nominal concentrations. The 72-hour EC_{50} values for mean cell density, specific growth rate and biomass area were >1958 mg/L. The 72-hour NOEC values for mean cell density, specific growth rate and biomass area were equal to 247 mg/L.

7.0 Human Health-Related Data

A data summary for DES is included in Table 1. The Robust Summaries are included in the IUCLID Dataset.

7.1 Acute Toxicity

Six male Wistar or Sherman strain rats were given a single dose by stomach tube of 10, 1, 0.1, etc. g/kg bw. The initial dose was judged by previous experience with this and other similar chemicals. One week later, six more animals were dosed at another concentration. This procedure was repeated until two dosages differing by a multiple of 10 were found, one of which killed all or some of the animals within 14 days and another which killed none or some of the animals in a 14 day period. The LD_{50} was then estimated on the assumption that the slope of the probit mortality vs. log dosage curve was the same as that of some structurally similar material previously studied (Smyth *et al.,* 1944). Using this method, the acute oral LD_{50} for DES was 880 mg/kg bw (Smyth *et al.*, 1949). Groups of six male Wistar or Sherman rats were exposed for two hours to a flowing stream of air saturated with vapors of DES, prepared by passing it through a fritted disc bubbler at room temperature. This procedure was repeated on naïve rats until two exposures were identified, one that resulted in 100% mortality and a second that resulted in 0% mortality within two weeks after inhalation (Smyth *et al.,* 1944). Inhalation of DES resulted in an LC_{50} between 250 (1275 mg/L) to 500 ppm (3150 mg/L) with no deaths at 250 ppm and 100% mortality at 500 ppm following four hours of exposure (Smyth *et al.,* 1949). Based on previous information on procedures used by the investigators, and the year of publication of the acute dermal toxicity study, while not confirmed, the following method is assumed to have been followed for the acute dermal toxicity study. Undiluted test material was applied to the clipped belly of an albino rabbit and the area was observed over 24 hours for necrosis, edema, erythema or congestion of capillaries. Initially, 0.01 µl of test material was applied, however, if a strong primary

reaction was elucidated, then the application was repeated on naïve animals with 10, 1.0 or 0.1%, etc. solutions as necessary to identify the lowest concentration causing irritation. The acute dermal LD_{50} was 706 mg/kg/bw (Smyth et al., 1944). These data are considered adequate to meet the HPV Chemical Challenge requirements.

7.2 Repeated Dose Toxicity

Repeated dose toxicity testing data are available as summarized for four carcinogenicity studies: two skin-painting studies, one oral gavage study, and one intravenous trans-placental carcinogenicity study. In spite of some study variances from guideline procedures, results of these studies indicate a potential for carcinogenicity, and the material is labeled accordingly. That is, repeated dermal application of undiluted DES over the life-span of the animals, produced malignant skin neoplasms in 21 mice out of a surviving effective group of 27 animals (Peterson, 1979). Based on these data, the consistent mutagenic response of DES (see below) and the classification of DES as a carcinogen, the production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals. With the stringency of carcinogenicity labeling already in place, The Dow Chemical Company believes that conducting additional repeated dose toxicity testing, with the attendant animal use, will not generate additional information which would increase safety data sheet or label warnings. Therefore, the available data are considered adequate to meet the HPV Chemical Challenge requirements.

7.3 Genetic Toxicity

7.3.1 *In vitro*

DES has been shown to be positive in the Salmonella preincubation reverse mutation assay (Ohtsuka and Maekawa, 1992). Although this study evaluated only one tester strain (TA100), the strong positive response precludes the need for additional testing. In this assay, DES resulted in a maximum of a 35-fold greater induction of revertants compared to the control with a clear dose response. No induction was observed at 500 µg/plate with a 6-fold increase at 1000 µg/plate and the 35-fold induction at 2000 µg/plate. DES has also been shown to be positive in mammalian cell assays. In the HGPRT mutation assay, CHO cells were exposed for 5 hours to concentrations of DES ranging from 80×10^{-3} to 5×10^{-3}% (by volume) without metabolic S-9 activation and from 40×10^{-3} to 2.5×10^{-3}% (by volume) with metabolic S-9 activation. The mutant fraction was determined after a 7- to 10-day period to allow "expression" of the mutant phenotype. Positive (ethylmethane-sulfonate [EMS] without metabolic activation and dimtheylnitrosamine [DMN] with metabolic activation), negative (cell medium) and solvent controls were also evaluated concurrently. A dose-related increase in induction of mutations with and without metabolic activation was observed in the CHO cells treated with DES (Slesinski *et al.*, 1980). The maximum response varied from 8 to 35-fold induction of mutations compared to the solvent control. The positive controls, dimethylsulfoxide (3700 µg/ml; with activation) and ethylmethanesulfonate (200 µg/ml; without activation), resulted in an approximately 10- and 9-fold induction of mutants, respectively, as compared to the solvent control. A sister chromatid exchange assay without metabolic activation also showed a dose-related increase in response with a maximum 2.5-fold increase in the number of SCE per chromosome (Slesinski *et al.*, 1980). In an unscheduled DNA synthesis assay, a non-dose related increase in DNA synthesis, as

measured by radioactive thymidine, was observed at all concentrations ranging from 0.0001 to 0.1% (v/v) (Slesinski *et al.*, 1980). The available data are considered adequate to meet the HPV Chemical Challenge requirements.

7.3.2 *In vivo*

Twelve male mice per group were administered DES intraperitoneally (i.p.; 100-400 mg/kg bw). DES increased the incidence of micronucleated erythrocytes in a mouse micronucleus assay at one time point (48 hours) at the highest single i.p. dose (400 mg/kg) tested (Asita *et al.*, 1992). In a second mouse micronucleus study in which five male and female mice per group were dosed with DES by i.p. injection, a positive effect at 30 hours was observed at 160 mg/kg of DES with no effect seen at 80 mg/kg (Hagashikuni and Shizuyo, 1995). A study using intrascrotal injection of DES resulted in dominant lethal effects (Malashenko, 1971). Although this study used a highly unusual dosing regimen, a second dominant lethal study is briefly reported as being positive using the more conventional intraperitoneal injection (Ehling and Neuhauser-Klaus, 1988). The available data confirm the biological activity of DES on the genome and are considered adequate to meet the HPV Chemical Challenge requirements.

7.4 Reproductive and Developmental Toxicity

There are no studies available for DES that evaluate potential reproductive or developmental toxicity. As noted above under "Section 5.2 – Stability in Water", DES is not stable at acid pH and would be expected to rapidly hydrolyze in the stomach. Therefore, surrogate data are useful for the HPV Chemical Challenge program, including results for dimethyl sulfate as well as ethanol and sulfuric acid.

There is a continuous breeding protocol study available for the closely related dimethyl sulfate (Bishop et al., 1997). The results of this study indicate a potential for dimethyl sulfate to interfere with fertility based on a reduction in the number of small ovarian follicles. In this same report, DES itself was injected into female mice and reproduction evaluated. A decrease in the number of offspring compared to controls was observed although, unlike dimethyl sulfate, there was no reduction in litters or effects on ovarian follicle counts. The two chemicals demonstrate similar toxicokinetic profiles; data from in vitro hydrolysis studies show that both hydrolyze to the alcohol (methanol or ethanol) and the substituent mono-alkyl sulfate initially, with potential further hydrolysis to additional alcohol and sulfuric acid.

For ethanol, a large body of data has been collected related to reproduction and, particularly developmental toxicity. The data are too voluminous to adequately review herein. The following is the conclusion from the SIAP (2004) for ethanol:

> *No fertility or developmental effects were seen at inhalation exposures up to 16000 ppm (30,400 mg/m3). The lowest reported NOAEL for fertility by the oral route was 2000 mg/kg bw in rats, equivalent to a blood alcohol concentration of 1320 mg/l, although this was based on a significant increase in the number of small pups rather than a direct effect on fertility; such direct effects are not seen until much higher doses. Many studies exist examining the developmental end point for ethanol. However, most use very high doses and*

> *few are individually robust enough to allow a NOAEL to be established. However, the collective weight of evidence is that the NOAEL for developmental effects in animals is high, typically >=6400mg/kg bw, compared to maternally toxic effects at 3600 mg/kg bw. The potential for reproductive and developmental toxicity exists in humans from deliberate over-consumption of ethanol. Blood ethanol concentrations resulting from ethanol exposure by any other route are unlikely to produce reproductive or developmental effects.*

Based on these conclusions, there is no potential for developmental effects from the hydrolysis of DES because it would not be possible to attain effect dose levels.

In addition, sulfuric acid is an ultimate hydrolysis product of DES. In a reproduction toxicity study with sulfuric acid, pregnant rabbits were exposed via inhalation for 7 hours a day over gestation days (gd) 6-18. The lowest toxic concentration (TCLo) was determined to be 20 mg/m^3 (IUCLID Dataset, 2/2000). In two developmental toxicity studies, no teratogenic effects were observed in CF-1 mice or New Zealand white rabbits exposed to sulfuric acid at concentrations of 0, 5 or 20 mg/m^3 via inhalation for 7 hours/day on gd 6-15 (mice) or gd 6-18 (rabbits). Little evidence of toxicity was observed in the fetuses of either species at any dose; while slight maternal toxicity was observed at the highest dose (Murray *et al.*, 1979).

Overall, based on results for the similar DMS and limited effects from DES, it is reasonable to conclude that DES may have minimal effects on reproductive capacity at high doses. DES would not be expected to result in developmental toxicity. The final hydrolysis products, sulfuric acid and ethanol, do not pose a reproductive or developmental hazard at potential doses from the hydrolysis of DES.

Finally, production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals. Further testing at higher doses in studies designed to evaluate reproductive and developmental toxicity, and/or identification of positive effects in such studies, will not alter the procedures and controls currently in place for the use and handling of DES. Therefore, the available data are considered adequate to meet the HPV Chemical Challenge requirements

8.0 Conclusion

Adequate information is available for melting point, boiling point, vapor pressure and partition coefficient, water solubility and hydrolysis for DES. Photodegradation and environmental distributions are adequately supported by the appropriate model data. Based on the results of hydrolysis testing, ecotoxicology studies were conducted on the hydrolysis product, ethanesulfuric acid which was found to be non-toxic to aquatic organisms at the highest concentration of 1000 mg/L. DES is biodegradable. In bacterial and mammalian cell systems and *in vivo* mutagenicity assays, DES is mutagenic, and it has been shown to be carcinogenic in animal studies. Based on data for a similar chemical, dimethyl sulfate, as well as the hydrolysis products, ethanol and sulfuric acid, DES poses only a minimal reproductive hazard at high doses. Production, labeling and handling of DES are specifically designed to minimize exposure to carcinogenic chemicals and are considered adequate for other potential toxic hazards. Therefore, the available data are considered adequate for the HPV Chemical Challenge Program.

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Table 1: HPV Data Summary

Sulfuric Acid, Diethyl Ester (Diethyl Sulfate)

CAS RN: 64-67-5		SPECIES	PROTOCOL	RESULTS
PHYSICAL-CHEMICAL				
2.1	Melting Point		Handbook Data (CRC)	-24.5 ºC
2.2	Boiling Point		Handbook Data (CRC)	208 ºC
2.4	Vapor Pressure		Handbook Data (DIPPR)	0.191 hPa (at 20 ºC)
2.5	Partition Coefficient (log K_{ow})		KOWWIN v. 1.67; UCC Unpub. Data	1.14
2.6	Water Solubility		Not specified	7000 mg/L
			Handbook Data (CRC)	Decomposes to ethanol and H_2SO_4;
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		AOPWIN v. 1.91	half-life: 6.5 days (OH Rate Constant)
3.1.2	Stability in Water		OECD 111	Hydrolysis to ethanesulfuric acid and ethanol (t1/2 < 0.4 hours at 25ºC) and ultimately to sulfuric acid and ethanol
3.3	Transport and Distribution		Mackay Level III 100% release to air	77% into atmosphere, 15% into water, 9% into soil, < 0.1% into sediment
			Mackay Level III 100% release to water	< 1% into atmosphere, 99% into water, < 0.1% into soil, < 1% into sediment
3.5	Biodegradation		BOD20	57% after 20 days
			OECD 301C	89% after 28 days
ECOTOXICOLOGY				
4.1	Acute/Prolonged Toxicity to Fish	*Oncorhynchus mykiss*	OECD 203	LC_{50} (96 hours) > 952 mg/L (ethane sulfuric acid was tested)
4.2	Acute Toxicity to Aquatic Invertebrates	*Daphnia magna*	OECD 202	EC_{50} (48 hours) > 914 mg/L (ethane sulfuric acid was tested)
4.3	Toxicity to Aquatic Plants e.g. Algae	*Pseudokirchneriella subcapitata*	OECD 201	EC_{50} (72 hours) > 952 mg/L (ethane sulfuric acid was tested)

Table 1: HPV Data Summary

Sulfuric Acid, Diethyl Ester (Diethyl Sulfate)

CAS RN: 64-67-5		SPECIES	PROTOCOL	RESULTS
TOXICOLOGY				
5.1.1	Acute Oral Toxicity	Rat		LD_{50} : 880 mg/kg bw
5.1.2	Acute Inhalation Toxicity	Rat		LC_{50} (4 hr): >250 ppm (1275 mg/L); <500 ppm (3150 mg/L)
5.1.3	Acute Dermal Toxicity	Rabbit		LD_{50} : 706 mg/kg bw
5.4	Repeated Dose Toxicity			See Text
5.5	Genetic Toxicity *In Vitro*			
	Bacterial Test (Gene mutation)	Salmonella typhimurium TA 100 only	Ames	Positive
		CHO	HGPRT -Similar to guideline	Positive
		CHO	SCE - Similar to guideline	Positive
		Rat	Hepatocyte UDS - similar to guideline	Positive
5.6	Genetic Toxicity *In Vivo*	Mouse	Micronucleus - Similar to guideline	Positive
		Mouse	Dominant lethal	Positive
5.8	Toxicity to Reproduction / Impairment of Fertility			See Text
5.9	Developmental Toxicity / Teratogenicity			See Text